K091260

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510(k) SUMMARY

Applicant:	Quest International, Inc. 8127 NW 29th Street Doral, FL 33122
Registration No.	1061839
Contact Person:	David J. Kiefer, Ph.D.,
Telephone:	(305) 592-6991
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Manufacturing Site:	Same as above
Device:	SeraQuest® EBV EA-D IgG
Device Name:	Epstein-Barr virus serological reagents (21CFR § 866.3235)
Device Classification:	Class I (general controls)

Description:

The SeraQuest EBV EA-D IgG Test is a solid-phase enzyme immunoassay (EIA), which is performed in microwells, at room temperature, in three thirty minute incubations. It has been developed to detect IgG antibodies which are directed against EBV Early Antigen D (EA-D), in human serum.

Principle:

Diluted samples are incubated in wells coated with EBV Early Antigen D. Antibodies directed against the antigen (if present) are immobilized in the wells. Residual sample is eliminated by washing and draining, and conjugate (enzyme-labeled antibodies to human IgG) is added and incubated. If IgG antibodies to EBV Early Antigen D are present, the conjugate will be immobilized in the wells. Residual conjugate is eliminated by washing and draining, and the enzyme substrate is added and incubated. In the presence of the enzyme, the substrate is converted to a yellow end-product which is read photometrically at 405 nm.

Intended Use:

The SeraQuest EBV EA-D IgG test is for the qualitative detection of human IgG antibodies to Epstein-Barr virus early antigen diffuse (EA-D) in human serum by enzyme immunoassay. This assay uses a 28 kd *E. coli* expressed recombinant Epstein-Barr virus early antigen. When performed in conjunction with other EBV serological tests, this assay can be used as an aid in the laboratory diagnosis of EBV infectious mononucleosis in patients with signs and symptoms of EBV infectious mononucleosis. For In Vitro Diagnostic Use Only.

Assay performance characteristics have not been established for neonatal, immunocompromised populations, cord blood, infants or pre-transplant patients. Assay performance characteristics have not been established for the diagnosis of nasopharyngeal carcinoma, Burkitt's lymphoma, and other EBV-associated lymphomas.

Predicate Device:

The SeraQuest® EBV EA-D IgG test is substantially equivalent in intended use and performance, to the Trinity Biotech Captia EBV EA-D IgG, Jamestown, NY.

Summary of technological characteristics:

Characteristic	SeraQuest EBV EA-D IgG	Trinity Biotech EBV EA-D IgG
Description:	Enzyme Immunoassay	Enzyme Immunoassay
Intended Use:	The detection of IgG antibodies against EBV EA-D in human serum.	The detection of IgG antibodies against EBV EA-D in human serum.
Solid Phase:	Plastic Microwell	Plastic Microwell
Antigen :	Recombinant EA-D 28 kd	Recombinant EA-D
Number of Incubation Periods:	Three	Four
Sample Dilution:	1:51	1:21
Sample Incubation Duration:	30 minutes	20 minutes

Incubation Temperature:	Room temperature	Room temperature
Ezyme-labeled Conjugate:		
Antibody	Goat anti-human IgG	Goat anti-human IgG
Label	Alkaline phosphatase	Horseradish Peroxidase
Conjugate Volume:	100 µl	100 µl
Conjugate Incubation Duration:	30 minutes	20 minutes
Substrate:	p-Nitrophenyl phosphate	TMB
Subtrate Volume:	100 µl	100 µl
Substrate Incubation Duration:	30 minutes	10 minutes
Stop Reagent:	0.5 M Trisodium phosphate	1M H2SO4,0.7M HCL
Stop Reagent Volume:	100 µl	50 µl
Readout:	Spectrophotometric 405 nm	Spectrophotometric 450 nm

Clinical Performance Comparison

Performance of the SeraQuest EBV EA-D IgG Test was evaluated against another commercially available EBV EA-D IgG ELISA test according to the EBV serological characterization of the specimens as determined by other EBV serological reagents. For purposes of classifying the EBV serological state, specimens were tested by reference EBV serology assays for EBV VCA IgG, EBV VCA IgM, and EBV EBNA-1 IgG. The EBV EA-D IgG result generated by the commercially available comparator EBV EA-D IgG ELISA test was not considered for purposes of characterizing the EBV serological state of the specimen. A total of 542 serum samples for which EBV serology tests were ordered was tested at 3 U.S. clinical testing sites. Of the 542 specimens, 477 were prospectively collected and prospectively tested specimens, and 65 were prospectively collected but retrospectively tested specimens to supplement the prospective study data. Of the 65 prospectively collected but retrospectively tested specimens, 50 were acute specimens and 15 were EBV seronegative specimens characterized by reference EBV serology assays for EBV VCA IgG, EBV VCA IgM, and EBV EBNA-1 IgG. Based upon the results of the three reference EBV serology tests, the specimens were categorized into one of four EBV serological state groups as indicated in Table 1 below.

Table 1: EBV serological state characterization

	Specimen Group				
EBV serological state	Prospectively Collected and Prospectively Tested	Prospectively Collected but retrospectively Tested	EBV VCA IgG	EBV VCA IgM	EBV EBNA-1 IgG
Acute	31	50			
			+	+	-
			-	+	-
EBV seronegative	60	15			
			-	-	-
Past Infection	311	0			
			+	-	+
Indeterminate	75	0			
			-	-	+
			+	-	-

			-	+	+
			+	+	+
Total	477	65	[redacted]		

+ reactive; - nonreactive;

Note: When a reference assay was equivocal, it was considered nonreactive (-).
The characterization by antibody response profile was not compared with clinical data regarding presence, absence or status of disease.

Using Table 1 as a guideline, testing results were analyzed by the SeraQuest EBV EA-D IgG Test and corresponding comparative EBV EA-D IgG ELISA test according to the EBV serological characterization based on EBV serology reference assays results. For the purpose of percent agreement calculations, SeraQuest EBV EA-D IgG test equivocal results were assigned to the opposite test result interpretation than that of the corresponding comparative test results. Likewise, the comparative test equivocal results were assigned to the opposite test result interpretation than that of the corresponding SeraQuest EBV EA-D IgG Test results.

Prospectively collected and prospectively tested 477 sample results from all three sites combined are summarized in Tables 2-3.

Table 2: SeraQuest EBV EA-D IgG Test vs. Comparator Assay: Comparison by EBV Serological Status Characterization

EBV Serological Classification	Comparator EBV EA-D IgG Interpretation									Total
	Positive			Equivocal			Negative			
	SeraQuest EBV EA-D			SeraQuest EBV EA-D			SeraQuest EBV EA-D			
	Pos	Equ	Neg	Pos	Equ	Neg	Pos	Equ	Neg	
	N	N	N	N	N	N	N	N	N	N
Acute	12	0	1	2	0	1	3	1	11	31
EBV	4	2	1	0	1	5	2	4	41	60
Past Infection	65	13	11	7	8	12	17	14	164	311
Indeterminate	16	3	5	0	3	4	6	2	36	75
Overall	97	18	18	9	12	22	28	21	252	477

Table 3: SeraQuest EBV EA-D IgG Test vs. Comparator Assay: Percent Agreement & Confidence Intervals by EBV Serological Status Characterization

EBV Serological Status	Positive Agreement		95% CI	Negative Agreement		95% CI
Acute Infection	12/14	85.7%	57.2-98.2	11/17	64.7%	38.3-85.8
EBV Seronegative	4/12	33.3%	9.9-65.1	41/47	87.2%	74.3-95.2
Past infection	65/101	64.4%	55.0-73.7	164/202	81.2%	75.8-86.6
Indeterminate	16/28	57.1%	37.2-75.5	36/44	81.8%	67.3-91.8
Overall	97/155	62.6%	55.0-70.2	252/310	81.3%	76.9-85.6

Prospectively collected but retrospectively tested 65 specimen results from Site A are summarized in Tables 4-5.

Table 4: SeraQuest EBV EA-D IgG Test vs. Comparator Assay: Comparison by EBV Serological Status Characterization

EBV Serological Classification	Comparator EBV EA-D IgG Interpretation									Total
	Positive			Equivocal			Negative			
	SeraQuest EBV EA-D			SeraQuest EBV EA-D			SeraQuest EBV EA-D			
	Pos	Equ	Neg	Pos	Equ	Neg	Pos	Equ	Neg	
	N	N	N	N	N	N	N	N	N	N
Acute	32	0	0	1	1	1	2	3	10	50
EBV	0	0	3	0	0	1	1	1	9	15
Overall	32	0	3	1	1	2	3	4	19	65

Table 5: SeraQuest EBV EA-D IgG Test vs. Comparator Assay: Percent Agreement & Confidence Intervals by EBV Serological Status Characterization

EBV Serological Status	Positive Agreement		95% CI	Negative Agreement		95% CI
Acute Infection	32/33	97.0%	84.2- 99.9	10/16	62.5%	35.4 – 84.8
EBV Seronegative	0/4	0%	0 – 60.2	9/11	81.8%	48.2 – 97.7
Overall	32/37	86.5%	71.2- 95.5	19/27	70.4%	49.8 – 86.2

In addition, test results generated by both the SeraQuest EBV EA-D IgG Test and the comparator EA-D IgG Assay relative to the actual EBV serological characterization of either acute infection, EBV seronegative or past infection, as determined by the

reference EBV serology assays for EBV VCA IgG, EBV VCA IgM, and EBV EBNA-1 IgG, for the 477 prospectively collected and tested specimens and the 65 prospectively collected but retrospectively tested specimens, are presented in Tables 6-7.

Table 6: Agreement of the Comparator EBV EA-D IgG Test, and the SeraQuest EBV EA-D IgG Test, relative to the EBV Serological Classification, for the prospectively collected and tested specimens

	Prospectively Collected and Tested			
	Comparator EBV EA-D IgG Test	95% CI	SeraQuest EBV EA-D IgG Test	95% CI
Positive Agreement (Acute Infection)	13/31 41.9%	24.5-60.9	17/31 54.8%	36.0-72.7
Negative Agreement (EBV Seronegative)	47/60 78.3%	65.8-87.9	47/60 78.3%	65.8-87.9
Negative Agreement (Past Infection)	195/311 62.7%	57.3-68.1	187/311 60.1%	54.7-65.6

Table 7: Agreements of the Comparator EBV EA-D IgG Test, and the SeraQuest EBV EA-D IgG Test, relative to the EBV Serological Classification, for the prospectively collected and retrospectively tested specimens

	Prospectively Collected and Retrospectively Tested			
	Comparator EBV EA-D IgG Test	95% CI	SeraQuest EBV EA-D IgG Test	95% CI
Positive Agreement (Acute Infection)	32/50 64.0%	49.2-77.1	35/50 70.0%	55.4-82.1
Negative Agreement (No Infection)	11/15 73.3%	44.9-92.2	13/15 86.7%	59.5-98.3

Cross-reactivity

The cross-reactivity study was designed to determine if samples from various disease states and other potentially interfering factors interfere with test results when tested with the SeraQuest EBV EA-D IgG Test. Specimens that were positive for various infectious diseases, heterophilic antibodies, autoimmune antibodies and antibodies against other EBV markers were tested with the SeraQuest EBV EA-D IgG Test. Samples for these

studies were selected using commercially available devices. Results can be found in Table 8.

Table 8: Cross-Reactivity

Analytes/Condition	Number of samples	Positive or Equivocal SeraQuest EBV EA-D IgG Test Result
Cytomegalovirus IgG	7	0/7
Herpes simplex virus 1&2 IgG	7	0/7
Varicella zoster virus IgG	11	0/11
Anti-Nuclear Antigen antibodies	2	0/2
Cytoplasmatic antigen SS-A antibodies	4	0/4
Cytoplasmatic antigen SS-B antibodies	4	0/4
Extractable nuclear antigen Sm antibodies	4	0/4
Cardiolipin IgG	6	0/6
Rheumatoid Factor	2	0/2
EBV VCA IgG	152	0/152
EBV VCA IgM	2	0/2
EBV NA antibodies	115	0/115
Total	316	0/316

None of the 316 total specimens tested in the cross-reactivity studies returned positive or equivocal results in the SeraQuest EBV EA-D IgG Test.

Warning: Potential cross-reactivity of the SeraQuest EBV EA-D IgG Test with IgG antibodies to *Toxoplasma gondii*, Rubella virus, HIV, HAV, HBV, and HCV was not tested and determined. The user is responsible for establishing cross-reactivity performance with these infectious agents.

Potential Interfering Substances

The possible effects of icterus, hemolysis, hyperglycemia, hyperlipidemia and hyperproteinemia, on the results of the SeraQuest EBV EA-D IgG test, were examined. A sample panel consisted of one weak positive serum sample (close to the assay cut-off) and one negative sample was prepared. Each serum specimen was first tested without any of the additive. This served as the control representing the normal physiological concentration of each of the potential interfering substances. In addition, aliquots of each serum specimen were supplemented with 8 times the normal level of each potential interferent. These levels were selected to exceed the levels that could be present in disease state sera. The normal and the "enriched" serum specimens with bilirubin, hemoglobin, glucose, cholesterol, and gamma globulin were tested following the SeraQuest EBV EA-D IgG Instructions for Use. Results can be found in Table 9.

Table 9: SeraQuest EBV EA-D IgG Test Results with Potential Interfering Substances

ANALYTE	ANALYTE CONCENTRATION			
	NORMAL		ELEVATED	
	POS (+) SAMPLE INDEX	NEG (-) SAMPLE INDEX	POS (+) SAMPLE INDEX	NEG (-) SAMPLE INDEX
BILIRUBIN	0.5 - 1.4 mg/dL		12 mg/dL	
	1.5	0.4	1.5	0.3
HEMOGLOBIN	0 gm/dL		18 gm/dL	
	1.4	0.4	1.3	0.4
GLUCOSE	60 -100 mg/dL		800 mg/dL	
	1.5	0.4	1.5	0.4
CHOLESTEROL	115 - 340 mg/dL		2,720 mg/dL	
	1.4	0.4	1.4	0.6
GLOBULIN	2.3 - 3.5 gm/dL		28 gm/dL	
	1.8	0.4	2.3	0.4

No significant interference was observed in the presence of up to eight times the normal physiological concentration of each of the potential interfering substances tested with the SeraQuest EBV EA-D IgG Test. There were no false negative results for the weak positive specimen and no false positive results for the negative specimens that were encountered in the presence of each of the potential interfering substances.

Warning: While the limited amount of data presented in the study above may not demonstrate it, serum specimens with elevated levels of these interfering substances may generate erroneous results. Grossly hemolyzed, icteric or lipemic samples as well as samples containing particulate matter or exhibiting obvious microbial contamination are not recommended and should not be tested

Precision

A reproducibility panel of 6 members was prepared by the Quest International laboratory. One (1) of the six panel members was negative for EBV EA-D IgG. One (1) of the 6 panel members had levels of EBV EA-D IgG near the assay cut-off that was considered a high negative to equivocal sample. Four (4) of the six panel members were positive for EBV EA-D IgG. All panel members were prepared from patient samples. This panel was split into aliquots and tested at 3 different clinical sites. In addition, 1 SeraQuest human Anti-EA-D IgG positive serum control and 1 SeraQuest human Anti-EA-D IgG negative serum control were also tested. Each of the 6 panel members and the SeraQuest positive and negative controls were tested three times (x3) on each day in one run for 3 days at each of the 3 US testing sites (3 times x 3 days x 3 sites = 27 replicates per panel member and SeraQuest control). The data was analyzed for intra-assay, inter-assay and between-site reproducibility. The standard deviation (SD) and percent coefficient of variation (%CV) were also calculated. Results can be found in Table 10.

Table 10: Reproducibility (Values were calculated from the SeraQuest index values.)

Name of analyte Panel Members	Sample N	Mean Index	Intra-Assay		Inter-Assay		Between-Site		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
SeraQuest Positive Serum Control	27	1.7	0.05	3.1	0.13	8.0	0.32	19.3	0.14	8.0
SeraQuest Negative Serum Control	27	0.4	0.01	4.1	0.04	9.1	0.07	21.0	0.03	8.4
High negative to equivocal (Near C.O.)	27	0.7	0.04	5.7	0.07	9.5	0.10	14.2	0.03	4.2
Negative	27	0.2	0.05	18.2	0.06	23.1	0.12	46.7	0.04	14.0
Positive 1	27	1.7	0.08	4.2	0.09	5.8	0.40	23.8	0.19	10.5
Positive 2	27	1.3	0.07	5.2	0.07	5.9	0.26	19.5	0.11	7.9
Positive 3	27	1.3	0.04	3.0	0.08	6.6	0.26	20.5	0.12	8.9
Positive 4	27	1.7	0.09	4.7	0.24	14.1	0.40	24.1	0.16	9.2

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Dr. David Kiefer
President
Quest International, Inc.
8127 N. W. 29th Street
Doral, FL 33122

JUN - 8 2009

Re: K091260
Trade/Device Name: SeraQuest EBV EA-D IgG Test
Regulation Number: 21 CFR 866.3235
Regulation Name: Multiple antibodies immunological test system
Regulatory Class: Class I
Product Code: LSE
Dated: April 3, 2009
Received: April 29, 2009

Dear Dr. Kiefer:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at 240-276-0450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at 240-276-3474. For questions regarding the reporting of device adverse events (Medical Device Reporting (MDR)), please contact the Division of Surveillance Systems at 240-276-3464. You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

Indication for Use

510(k) Number: k091260

Device Name: SeraQuest EBV EA-D IgG

Indication For Use:

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Prescription Use X And/Or Over the Counter Use ____.
(21 CFR Part 801 Subpart D) (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) k091260